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EXAMINER

LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 04/12/2002

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/402,277

Applicant(s)

KAWASHIMA ET AL.

Examiner

Frank Lu

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 and 59-64 is/are pending in the application.
- 4a) Of the above claim(s) 59-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 December 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Detailed Action*.

Art Unit: 1655

DETAILED ACTION

Response to Amendment

1. Applicant's response to the final office action filed on November 16, 2002 has been entered as Paper No: 21. The claims pending in this application are claims 1-26 and 59-64 with claims 59-64 withdrawn from consideration as the result of the restriction requirement.

Election/Restriction

2. Applicant's election with traverse of Group I, claims 1-26 in Paper No. 21 is acknowledged. The traversal is on the ground(s) that: (1) "[T]raversal is based on claims 1-26 and 59-64 being linked so as to form a single general invention concept under PCT Rule 13.1."; (2) "it would be premature at this time to find that the claims are not novel and nonobvious." even "the examiner cites Adams et al. in support of his assertion that the claimed method and apparatus do not distinguish over the prior art," ; (3) "[D]elay the examination of claims 59-64 would not be in the public interest and does not result in compact prosecution."; and (4) "[I]t does not constitute an undue burden to continue examination of claims 1-26 and 59-64 as amended." since "the Examiner has already searched, examined, and issues an Office Action for the claimed method and apparatus."

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that Groups I and II will be examined together.

Art Unit: 1655

First, as shown in pages 2 and 3 of previous office action, the examiner clearly explained why claims 1-26 and 59-64 were not linked so as to form a single general invention concept under PCT Rules 13.1 and 13.2. “[D]elay the examination of claims 59-64 would not be in the public interest and does not result in compact prosecution.” was not the reason for the restriction requirements.

Second, the examiner did not agreed with applicant that it might be premature to cite a prior art in *Election/Restriction* to show that the claims are not novel and nonobvious because the examiner did study this patent before applying it in *Election/Restriction*. Furthermore, the purpose that the examiner cited a prior art was not only to show that claims 1-26 and 59-64 are not linked so as to form a single general invention concept under PCT Rules 13.1 and 13.2, but also to inform applicant that a prior art found by the examiner could be used for later reactions. By this way, applicant could amend claims and prevent the examiner to use this prior art for rejections so that the office could speed the prosecution of this instant application. Unfortunately, applicant did not amend claims and the examiner need use this prior art for rejections in this office action.

Third, although “the Examiner has already searched, examined, and issues an Office Action for the claimed method and apparatus.”, the examiner have reasonably withdrawn previous final rejection and reopen prosecution. A reopened prosecution will need a new search and give the examiner another chance to reconsider previous decision he made. Since claims 1-26 and 59-64 were not linked so as to form a single general invention concept (see previous office action), the restriction requirement is still deemed proper and is therefore made FINAL.

Art Unit: 1655

Drawings

3. The drawings submitted on December 28, 2000 are still objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Specification

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

5. Claim 8 is objected to because of the following informality: "two different types of primer" in line 2 should be "two different types of primers".

6. Claim 9 is objected to because of the following informality: " 2" different types of primer" in line 2 should be "2" different types of primers".

7. Claim 23 is objected to because of the following informality: there is no period in the end of the claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1655

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 3, 4, 13, 18, 20, and 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claims 25 and 26 are dependent on claim 23.
10. Claims 3 and 4 are rejected as vague and indefinite over the phrase "a given nucleic acid sequence to be amplified (which sequence may be known or unknown) to which have been added a first nucleic acid sequence and a second nucleic acid sequence" because it is unclear what it intended. For example, does this phrase mean that a given nucleic acid sequence to be amplified further comprises a first nucleic acid sequence and a second nucleic acid sequence or mean something else?
11. Regarding claim 13, the phrase "e.g. in a grid pattern" is similar to "for example" that renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).
12. Regarding claim 18, the phrase "e.g. fluorescent labels or radiolabels" is similar to "for example" that renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).
13. Claim 20 is rejected as vague and indefinite because it is unclear what it intended. For example, comparing the limitations among claims 1, 19, and 20, it is unclear which step in claim 1 is performed before a cleavage step recited in claim 19. If the cleavage step is performed directly after step B) of claim 1, steps C) to E) could not be finished since the target nucleic acid

Art Unit: 1655

cleaved by a restriction endonuclease or ribozyme may lose its ability to hybridize with immobilized primers (lose a sequence that hybridizes with the primers). Please clarify.

14. Claims 23 and 24 are rejected as vague and indefinite because it is unclear what it intended. For example, does these claims mean to amplify a plurality of different nucleic acid sequences using a target nucleic acid as a template or using a plurality of different target nucleic acids as templates?

15. Claim 25 is rejected as vague and indefinite the phrase "said first and second nucleic acid sequences being the same for the each of the different nucleic acid sequences" because it is unclear what it intended. For example, if each of the different nucleic acid sequences is consist of a first and a second nucleic acid sequences wherein the first and second nucleic acid sequences are identical, each of the different nucleic acid sequences will be identical and there will be no different nucleic acids. Please clarify.

Claim Rejections - 35 USC § 102/103

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Art Unit: 1655

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-24 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Adams *et al.*, (WO 96/04404, published on February 15, 1996).

Regarding claims 1, 2, 7, 14-19, and 22, as shown in Figures 2A to 2L, Figure 3, and example 3, Adams *et al.*, taught a method for performing amplification of nucleic acid on supports. In this method, a target nucleic acid (first nucleic acid) first hybridized with one or more of plurality of identical primers recited in claim 7 (second nucleic acid, see last paragraph in page 25) that had a sequence complementary to the target sequence and was covalently linked to the support, and then PCR (denaturation at 94⁰ C as recited in claim 15, annealing at 55⁰ C and extension at 75⁰ C) was performed using the target nucleic acid as a template in the presence of

Art Unit: 1655

thermostable polymerase, enzyme buffer, labeled and unlabeled DNTP in an automated instrument as recited in claim 22 (see page 18, third paragraph). During the PCR cycles (for example, 30 cycles, see example 2 in page 24), the amplified products from the early cycles were annealed with different sets of identical primers in latter cycles as recited in steps D) and E) of claim 1 and steps F) and G) of claim 2 (see pages 5-7, and 17-26).

Regarding claims 3-5 and 8-10, Adams *et al.*, taught that two different types of primer were immobilized on a support. For example, as shown in Figure 1B, a target double stranded nucleic acid (first nucleic acid 23) comprised a first strand 25 and a second strand 27 and each strand had two target sequences a and b at their 3' and 5' ends recited in claim 5. Second nucleic acid 13 (primer) was complementary to target sequence a of strand 25 and third nucleic acid 15 (primer) was complementary to sequence b of strand 27 (both second and third nucleic acids were immobilized on a support and served as primers) (see pages 14-17 and Figures 1A to 1M). Note that : (1) if n was equal to zero in claim 9, claims 9 and 10 were identical; (2) in Figure 1G, a and b of the first strand 25 could be considered as the first nucleic acid sequence that hybridized with primer 13 and the second nucleic acid sequence that hybridized with a sequence (31) recited in claim 3; and (3) since third nucleic acid 15 (primer) was complementary to sequence b of strand 27 and the first strand 25 and the second strand 27 were plus and minus strands of target double stranded nucleic acid (first nucleic acid 23), sequence b of strand 25 should be identical to third nucleic acid 15 (primer) as recited in claim 4.

Regrading claim 11, the different primers had about the same concentrations (see example 2, page 24, last paragraph).

Art Unit: 1655

Regarding claims 12 and 13, the primers were homogeneously dispersed over a given area and be located in a predetermined arrangement (see Example 6, page 28, second paragraph).

Regarding claims 20 and 21, PCR products amplified with primers with a restriction endonuclease site were released by cleavage with the restriction endonuclease(see pages 32 and 33).

Regarding claims 23 and 24, although Adams *et al.*, did not teach to amplify a plurality of different nucleic acid sequence, the uses of the method of claim 1 as recited in claims 23 and 24 could be considered as intended uses. Note that it is well known that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963).

Therefore, Adams *et al.*, teach all limitations recited in claims 1-24.

19. Claims 1-6, 8-10, and 12-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Adams et al., (US Patent No., 6,060,288, filed on February 14, 1997).

Regarding claims 1, 2, 14-19 and 22, as shown in Figures 2A to 2L, Figure 3 and example 1, Adams *et al.*, taught a method for performing amplification of nucleic acid on supports. In this method, a target nucleic acid (first nucleic acid) first hybridized with one or

Art Unit: 1655

more of plurality of primers that had a sequence complementary to the target sequence and was covalently linked to the support, and then PCR (denaturation at 94° C as recited in claim 15, annealing at 55° C and extension at 75 ° C) was performed using the target nucleic acid as a template in the presence of thermostable polymerase, enzyme buffer, labeled and unlabeled DNTTP in an automated instrument as recited in claim 22 (see column 10). During the PCR cycles (for example, 30-100 cycles, see example 2 in columns 22 and 23), the amplified products from the early cycles were annealed with different sets of identical primers in latter cycles as recited in steps D) and E) of claim 1 and steps F) and G) of claim 2 (see column 1-3 and 10-12).

Regarding claims 3-5 and 8-10, Adams *et al.*, taught that two different types of primer were immobilized on a support. For example, as shown in Figure 1B, a target double stranded nucleic acid (first nucleic acid 23) comprised a first strand 25 and a second strand 27 and each strand had two target sequences a and b at their 3' and 5' ends recited in claim 5. Second nucleic acid 13 (primer) was complementary to target sequence a of strand 25 and third nucleic acid 15 (primer) was complementary to sequence b of strand 27 (both second and third nucleic acid were immobilized on a support and served as primers) (see columns 8-10 and Figures 1A to 1M). Note that : (1) if n was equal to zero in claim 9, claims 9 and 10 were identical; (2) in Figure 1G, a and b of the first strand 25 could be considered as the first nucleic acid sequence that hybridized with primer 13 and the second nucleic acid sequence that hybridized with a sequence (31) recited in claim 3; and (3) since third nucleic acid 15 (primer) was complementary to sequence b of strand 27 and the first strand 25 and the second strand 27 were plus and minus

Art Unit: 1655

strands of target double stranded nucleic acid (first nucleic acid 23), sequence b of strand 25 should be identical to third nucleic acid 15 (primer) as recited in claim 4.

Regarding claims 12 and 13, the primers were homogeneously dispersed over a given area and be located in a predetermined arrangement (see Example 3, example 3, column 23).

Regrading claims 21 and 22, PCR products amplified with primers with a restriction endonuclease site were released by cleavage with the restriction endonuclease (see column 26).

Regarding claims 23-24, Adams *et al.*, taught multiplex PCR in the presence of different target nucleic acid sequences (see columns 3-5).

Therefore, Adams *et al.*, teach all limitations recited in claims 1-6, 8-10, and 12-24.

20. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams *et al.*, (1997) as applied to claims 1-6, 8-10, and 12-24 above, and further in view of Schumn *et al.*, (US Patent No., 5,843,660, filed on April 15, 1996).

The teachings of Adams *et al.*, (1997) have been summarized previously, *supra*. Adams *et al.*, teach to incorporate a fluorescence label into a amplification product (see column 4).

Adams *et al.*, do not disclose to use different fluorescent tags in order to distinguish different amplified products.

Schumn *et al.*, do teach to use different fluorescent tags in order to distinguish different amplified products. For example, see column 3, Examples 19 and 20 in column 29 and Figures 19 and 20.

Art Unit: 1655

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed multiplex PCR using different target nucleic acids as templates in the presence of different fluorescent tags in view of the patents from Adams *et al.*, and Schumn *et al.*. One having ordinary skill in the art would have been motivated to modify the methods of Adams *et al.*, and combine above methods together in order to distinguish different amplified products because Schumn *et al.*, suggested that different fluorescent tags in multiplex PCR were used to distinguish different amplified products (see column 3). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to distinguish different amplified products using different fluorescent tags.

Conclusion

21. No claim is allowed.
22. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.


Art Unit: 1655

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
March 29, 2002



ETHAN C. WHISENANT
PRIMARY EXAMINER